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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,939	04/11/2006	Christophe Revirron	05-403	8331

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	**PAPER NUMBER**
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,939	REVIRRON, CHRISTOPHE	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 22-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10 and 22-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments, IDS and remarks received in the office on 10/22/2007. Claims 1-9, 11-21 have been canceled. Claims 10, 22-29 are pending and are being examined on the merits herein.

Response to Remarks

Applicants' arguments regarding the rejection of claims 10, 22, 23, 25-28 under 35 U.S.C. 103(a) as being unpatentable over Gensthaler (Pharmazeutische Zeitung, vol. 146, no. 7, 2001-02-15, p 35-36) in view of Leynadier et al (Acta Otorhinolaryngol Belg. 2001, 55(4): 305-12) have been fully considered and found not persuasive. Applicants' arguments regarding the rejection of claims 10, 22-29 under 35 U.S.C. 103(a) as being Salmun et al. (US 2003/0236275) have been fully considered and found not persuasive. Accordingly, the rejections are maintained and given in this office action for Applicants' convenience. Thus the office action is made Final.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10, 22, 23, 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gensthaler (Pharmazeutische Zeitung, vol. 146, no. 7, 2001-02-15, p 35-36) in view of Leynadier et al (Acta Otorhinolaryngol Belg. 2001, 55(4): 305-12).

Gensthaler teaches that Levocetirizine was effective in the treatment of patients with seasonal allergic rhinitis (p 35, para 4 lines 1-2). The reference further teaches an intended study of the long-term effect of Levocetirizine in 500 adults with persistent allergic rhinitis (p 36, lines 3-8).

The reference does not teach a method of administration in a daily dosage of about 0.0005 mg to about 2 mg per kg of body weight in treating persistent allergic rhinitis patients or the number of dosages in the intended study of persistent allergic rhinitis.

Leynadier et al teaches a dosage of 2.5, 5, 10 mg/day of levocetirizine by oral administration in a method of treatment for seasonal allergic rhinitis with symptoms such as sneezing, rhinorrhea, nasal congestion, nasal pruritus, ocular pruritis, itchy nose and itchy eyes. For example, administration of 2.5, 5 and 10 mg of Levocetirizine to a 20 kg patient would amount to 0.125 mg/kg, 0.25 mg/kg, and 0.5 mg/kg of body weight, which falls within the range claimed in claims 21 and 22.

It would have been obvious to one of ordinary skill in the art to administer levocetirizine in the treatment of persistent allergic rhinitis because Gensthaler teaches the effectiveness of the compound in seasonal allergic rhinitis and further teaches the intended clinical study of persistent allergic rhinitis with the same compound. Hence one of ordinary skill in the art would have been motivated to administer levocetirizine in the treatment of persistent allergic rhinitis to obtain similar therapeutic benefits. It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to administer a dose of 0.0005 mg to about 2 mg per kg of body weight per patient for

the treatment of persistent allergic rhinitis. Leynadier et al. teaches range of dosages of levocetirizine administered to subjects suffering from rhinitis. One of ordinary skill in the art would have been motivated to adjust the dosage amount or dosages administered per day by routine experimentation as one can expect similar therapeutic benefits and safety in the administration of levocetirizine to patients with persistent allergy as Leynadier has shown the drug to be safe and therapeutically beneficial in the patients with seasonal allergy rhinitis.

Claims 10, 22-29 are rejected under 35 U.S.C. 103(a) as being Salmun et al. (US 2003/0236275).

Salmun et al. teaches antihistamines such as levocetirizine, desloratadine are useful in the treatment of seasonal allergic rhinitis. The reference teach desloratadine has the added benefit of providing significant relief from persistent allergic symptoms such as nasal congestion/stuffiness in patients with seasonal allergic rhinitis (p 4, para 0050). The reference further teaches a dosage of 2.5 mg to about 45 mg/day of desloratadine in the treatment of allergic and inflammatory conditions (p 2, para 0026) will fall in the range of 0.05 mg/kg to 0.9-mg/kg body weight when administered to a patient weighing 50 kg. The reference also teaches different modes of administration such as topical, inhalation, oral etc. (p 3, para 0037).

The reference does not explicitly teach levocetirizine or desloratadine in the treatment of persistent allergic rhinitis or multiple dosage administration of levocetirizine or the period of administration to be 3 months or more.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer levocetirizine in a method of treatment for persistent allergic rhinitis because of the teachings of Salmun et al. The reference teaches desloratadine, an antihistamine has the added benefit of providing significant relief from persistent allergy symptoms such as nasal congestion/stuffiness in patients with SAR. It would have been obvious to one of ordinary skill in the art at the time of the invention to administer an antihistamine such as desloratadine or levocetirizine in a method of treatment for persistent allergic rhinitis as Salmun et al. teaches that the antihistamine compound provide significant relief of persistent allergy symptoms such as nasal congestion/stuffiness. Hence one of ordinary skill in the art would have been motivated to achieve similar or superior therapeutic benefits by the administration of levocetirizine to persistent allergy patients. One of ordinary skill in the art at the time of the invention would have been motivated to optimize the parameters such as multiple dosage administration of levocetirizine or period of administration for 3 or more months by routine experimentation as Salmun et al have taught the administration of levocetirizine to be safe and beneficial in rhinitis patients.

Response to Arguments

Applicants' argue that Gensthaler's teachings of treatment of seasonal allergic rhinitis (SAR) do not render the claims obvious because, at the time of filing, SAR was recognized as not being descriptive of a single, well characterized condition and the results of treating with levocetirizine patients previously characterized as suffering from SAR were not considered to be sufficiently predictive of the results of using

levocetirizine to treat patients suffering from PER. In response, Gensthaler teach SAR and persistent allergic rhinitis (PER) to be two different conditions as they show evidence from clinical trials on patients with SAR the effectiveness and safety of levocetirizine and further state their intention to conduct a study with patients suffering from persistent allergic rhinitis with the same drug Xusal (levocetirizine). Also, Gensthaler define that according to the new WHO definition, reference is made to this clinical condition if symptoms are present more than four days a week and for more than four weeks. According to the ARIA workshop document (The J of Allergy and Clinical Immunology, Vol. 108, 5, Nov 2001, IDS, Applicant cited reference) persistent allergic rhinitis is defined as "when the symptoms are present more than 4 days a week, and for more than 4 weeks" (p S148, Table 1) and the symptoms of persistent rhinitis is listed as obstruction, sneezing and rhinorrhea. The symptoms of intermittent rhinitis is listed as obstruction, sneezing and profuse rhinorrhea (P S 190, Figure 12). Leynadier et al teaches a method of treatment for seasonal allergic rhinitis with symptoms such as sneezing, rhinorrhea, nasal congestion, nasal pruritus, ocular pruritis, itchy nose and itchy eyes. Hence it would have been obvious to one of ordinary skill in the art from the teachings of Gensthaler and Leynadier that SAR and PER are two different clinical conditions with symptoms in common. It would have been obvious to one of ordinary skill in the art at the time of the invention to administer levocetirizine in a method of treatment for persistent allergic rhinitis from the studies of Gensthaler. One of ordinary skill in the art would have been motivated in expectation of success in effectively relieving symptoms associated with the persistent allergic rhinitis condition.

Applicants' argue that Gensthaler does not provide an enabling disclosure and the reference merely informs an intent to conduct a study on the use of levocetirizine for the treatment of patients with PER. In response, Though Gensthaler does not provide an enabling disclosure the teachings provide motivation to one of ordinary skill in the art to administer levocetirizine in the treatment of persistent allergic rhinitis as Gensthaler teaches the effectiveness of the compound in seasonal allergic rhinitis and further teaches the intended clinical study of persistent allergic rhinitis with the same compound.

Applicants' argue that Leynadier or Gensthaler does not teach dosage or routes of administration effective for the treatment of persistent allergic rhinitis. In response, reference teaches the same compound levocetirizine as claimed in the instant application and the dosages in the treatment of seasonal allergy rhinitis. Though the allergies, seasonal and persistent are distinct in nature as pointed out by the Applicants' they belong to the same class (allergies) and hence one of ordinary skill in the art would have been motivated to have a reasonable expectation of success by administering the same dosages or varying the amount of dosages (using Leynadier's teachings as a reference) by routine optimization. It would have been customary for an artisan of ordinary skill to determine the optimal amount of ingredient to add in order to best achieve the desired results.

Applicants' state in their arguments that because of the uncertainties prior to the trial (and prior to the present invention) the results achieved were not predictable. In response, levocetirizine has been shown to be effective in the prior art in a method of

treatment of SAR and there are symptoms common between PER and SAR. The results achieved by the instant application would have been predictable because the prior art teach that both SAR and PER are allergic rhinitis clinical conditions and the drug has been shown to be effective in the treatment of SAR that has symptoms common such as obstruction, sneezing and rhinorrhea to PER.

Applicants' state that Salmun never mentions PER in the definition of allergic and inflammatory conditions and thus Salmun is not referring to PER but persistent symptoms of SAR. In response, the rejection in the previous office states that Salmun reference teaches desloratadine, an antihistamine has the added benefit of providing significant relief from persistent allergy symptoms such as nasal congestion/stuffiness in patients with SAR. Hence the persistent allergic symptoms in SAR has not been confused with PER. However, it would have been obvious to one of ordinary skill in the art at the time of the invention that a drug capable of treating persistent symptoms in SAR a related clinical allergic rhinitis conditions with common symptoms to PER would be useful in a method of relieving PER, a clinical condition with symptoms that persist longer. . One of ordinary skill in the art at the time of the invention would have been motivated to optimize the parameters such as multiple dosage administration of levocetirizine or period of administration for 3 or more months by routine experimentation as Salmun et al have taught the administration of levocetirizine to be safe and beneficial in rhinitis patients.

Conclusion

No claims are allowed.

The rejections from the previous office action are maintained. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER